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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,122	08/08/2005	Gary A. Clawson	14017-008US1/PSU 2002-266	4883

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,122	CLAWSON ET AL.	
	Examiner	Art Unit	
	/Sean R. McGarry/	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *8-10,18,19,30,36,37 and 40-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11-17,20-29,31-35,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/05/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 8, 18, 19, 30, 36, 37, and 40-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/25/07. Claims 9 and 10 are also withdrawn since it is not agreed that they encompass the elected species. Kertatolytic agents are used for the delivery of agents to skin such as for warts. It is noted that HPV-16 , the elected HPV, is not associated with the use of such delivery agents as they[agents to inhibit HPV-16] would be delivered to the cervix and not to skin, for example. The examiner provides at the end of this Official Action, however, reference that would be relevant to such carriers.

Claims 1-7, 11-17, 20-29, 31-35 and 38-39 are under examination and furthermore, upon reconsideration the examiner will examine both siRNA and antisense in the elected invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 11-14, 16, 17, 20, 23-29, 34, 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Crooke et al [US 6,174,870].

Crooke et al disclose the use of antisense oligonucleotides to inhibit HPV16 in human cells and in humans (see claims 8-14, for example). At columns 1, and 4; and claim 14, for example, it is disclosed that cervical intraepithelial neoplasias as well as various other conditions are treated with antisense to HPV 16. At column 15, for example, it is disclosed to apply antisense compositions against HPV topically or interlesionally. It is noted that the recited means by which the antisense agents/targets of the invention are selected for provides no required structural difference between the compound of the prior art and the compounds used in the instant invention. It is the position of the examiner that the compounds of the prior art could be identified by a library selection, for example.

Claims 31-33 and 38-39 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Crooke et al [US 6,174,870].

Crooke et al disclose the use of antisense oligonucleotides to inhibit HPV16 in human cells and in humans (see claims 8-14, for example). At columns 1, and 4; and claim 14, for example, it is disclosed that cervical intraepithelial neoplasias as well as

various other conditions are treated with antisense to HPV 16. At column 15, for example, it is disclosed to apply antisense compositions against HPV topically or interlesionally.

Crooke et al do not specifically disclose by what percent the HPV is reduced in their methods and also do not teach whether the HPV is integrated or replicating. The examiner cannot determine these limitations since the Office is not equipped to make such an evaluation. However, even if the limitations are not met by the reference it would have been obvious to meet the limitations for the following reasons. One in the art clearly knows that HPV is inhibited by antisense and also knows that conditions where cells are infected with HPV (a cervical intraepithelial neoplasia) contain integrated and non integrated and replicating and nonreplicating virus a various points of the diseases or conditions progression. It would be obvious to treat such a disease once it was detected, regardless of the state of the virus at any given moment. Clearly one would be motivated to start a treatment as soon as possible and for a duration of sufficient length to eliminate as much virus as possible. Since the goal of treatment is to eliminate a virus 100% it would clearly be an optimization to eliminate a level (25, 50 or 75% on the road to total elimination. The invention as a whole, if not anticipated, would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

**A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION,
AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE
APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE**

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Claims 1-3, 7, 16, 20, 23-25, 29, and 34 rejected under 35 U.S.C. 102(e) as being anticipated by Milner et al [US 2004/0235171 A1].

Milner et al disclose the inhibition of HPV-16 in human and human cells for the treatment of cervical carcinoma via siRNA. See paragraphs [0011], [0036], [0057], [0068], [0092], [0096]-[0098], [0100] and claims 18-27, for example. It is noted that the recited means by which the siRNA agents/targets of the invention are selected for

provides no required structural difference between the compounds of the prior art and the compounds used in the instant invention. It is the position of the examiner that the compounds of the prior art could be identified by a library selection, for example.

Claims 31-33 and 38-39 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Milner [US 2004/0235171].

Milner et al disclose the inhibition of HPV-16 in human and human cells for the treatment of cervical carcinoma via siRNA. See paragraphs [0011], [0036], [0057], [0068], [0092], [0096]-[0098], [0100] and claims 18-27, for example.

Milner does not specifically disclose by what percent the HPV is reduced in her methods and also do not teach whether the HPV is integrated or replicating. The examiner cannot determine these limitations since the Office is not equipped to make such an evaluation. However, even if the limitations are not met by the reference it would have been obvious to meet the limitations for the following reasons. One in the art clearly knows that HPV is inhibited by antisense and siRNA and also knows that conditions where cells are infected with HPV (a cervical intraepithelial neoplasia) contain integrated and non integrated and replicating and nonreplicating virus at various points of the diseases or conditions progression. It would be obvious to treat such a disease once it was detected, regardless of the state of the virus at any given

moment. Clearly one would be motivated to start a treatment as soon as possible and for a duration of sufficient length to eliminate as much virus as possible. Since the goal of treatment is to eliminate a virus 100% it would clearly be an optimization to eliminate a level (25%, 50% or 75%) on the road to total elimination. The invention as a whole, if not anticipated, would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

> **A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION,
> AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE
> APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE**
>
> **"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).**

**A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE
PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC**

**Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35
U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.**

**A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION,
AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE
APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE**

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70,

205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 11-16, 20, 23-29, 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Milner et al [above], and Crooke et al [above].

The rejected invention is as set forth in the claims limited to treatment with siRNA.

Milner et al disclose the inhibition of HPV-16 in human and human cells for the treatment of cervical carcinoma via siRNA. See paragraphs [0011], [0036], [0057], [0068], [0092], [0096]-[0098], [0100] and claims 18-27, for example. Milner has not specifically taught the topical application of siRNA, specifically naming CINI-III, or specifically stating where the carcinoma is localized.

Crooke et al disclose the use of antisense oligonucleotides to inhibit HPV16 in human cells and in humans (see claims 8-14, for example). At columns 1, and 4; and claim 14, for example, it is disclosed that cervical intraepithelial neoplasias as well as various other conditions are treated with antisense to HPV 16. At column 15, for

example, it is disclosed to apply antisense compositions against HPV topically or interlesionally.

One in the art would have known that the topical application of siRNA was a mode of choice since the prior art has already shown the delivery of other nucleic acid drugs by this mode. One in the art would clearly have recognized also that any disease treatable by inhibiting HPV-16 would be treatable by siRNA as Crooke et al have at least identified by name cumulative types of neoplasia and carcinomas, for example. In fact Milner et al acknowledge the use of antisense and ribozymes for treating HPV infections and assert that siRNA is a better agent, see paragraph [0096], for example.

It is noted that the recited means by which the siRNA agents/targets of the invention are selected for provides no required structural difference between the compounds of the prior art and the compounds used in the instant invention. It is the position of the examiner that the compounds of the prior art could be identified by a library selection, for example.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

Claims 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke et al and Milner above, and further in view of the following explanation.

The claimed invention is as is a method of inhibiting HPV-16 in cells in a mammal such as an immunodeficient mouse with human cells infected with HPV-16 therein.

The Crooke and Milner references are relied upon as in all of the rejections above. The references do not teach inhibiting HPV-16 in an experimental model as claimed. However it would be clearly obvious to use an established model such as nude or scid mice that have been used for xenograft experiments for decades. These models provide data for drug selection by enabling on in the art to test their drug in a growing tumor instead of in transformed cells in culture providing for more relevant study of the drug.

Since these models are well established tools for testing tumor drugs and the claimed invention is for the treatment of tumors it is clear that such an embodiment would have been obvious to one developing drugs for the treatment of HPV induced tumors.

The invention as a whole would therefore have been *prima facie* obvious to one in the art at the time the invention was made.

The following prior art is made of record and not relied upon, but is considered pertinent to applicant's disclosure. US 6,821,523, US 6,896,888, and US 5,053,024.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to /Sean R. McGarry/ whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on (571) 272-0763. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean R McGarry/
Primary Examiner
Art Unit 1635